USSN10/009,852 Restriction Requirement dated 12 Aug 2004 Response dated 27 August 2004

Please replace the indicated claim below with the amended claim of the same number.

J. 3

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-91. (Previously canceled).

- 92. (previously presented) An isolated nucleic acid molecule, comprising
- (a) a nucleotide sequence encoding a vascular endothelial growth factor (VEGF) receptor component consisting essentially of an immunoglobulin-like (Ig) domain 2 of a first VEGF receptor and Ig domain 3 of a second VEGF receptor; and
 - (b) a nucleotide sequence encoding a multimerizing component.
- 93. (Previously presented) The isolated nucleic acid molecule of claim 92, wherein the first VEGF receptor is Flt1.
- 94. (Previously presented) The isolated nucleic acid molecule of claim 92, wherein the second VEGF receptor is Flk1 or Flt4.
- 95. (Previously presented) The isolated nucleic acid molecule of claim 92, wherein the nucleotide sequence encoding a first VEGF receptor component is upstream of the nucleotide sequence encoding a second VEGF receptor component.
- 96. (Previously presented) The isolated nucleic acid molecule of claim 92, wherein the nucleotide sequence encoding a first VEGF receptor component is downstream of the nucleotide sequence encoding a second VEGF receptor component.
- 97. (Previously presented) The isolated nucleic acid of claim 92, wherein the multimerizing component comprises an immunoglobulin domain.
- 98. (currently amended) The isolated nucleic acid of claim 97, wherein the immunoglobulin domain is selected from the group consisting of the Fc domain of IgG, and the heavy chain of IgG, and the light chain of IgG.
- 99. (Previously presented) The isolated nucleic acid molecule of claim 92, comprising a nucleic acid sequence selected from:
 - (a) SEQ ID NOs:3, 5, 7, 9, 11, 13, or 15; and
- (b) nucleic acid sequences which, as a result of the degeneracy of the genetic code, differ from the nucleic acid sequence of SEQ ID NOs:3, 5, 7, 9, 11, 13, or 15.
- 100. (Previously presented) The isolated nucleic acid molecule of claim 92, wherein the components of the fusion polypeptide are arranged as 1,2,3; 1,3,2; 2,1,3; 2,3,1; 3,1,2; or 3,2,1, wherein 1 is the first VEGF receptor component, 2 is the second VEGF receptor component, and 3 is the multimerizing component.

- 101. (Previously presented) A fusion polypeptide encoded by the nucleic acid molecule of claim 92.
- 102. (Previously presented) A pharmaceutical composition, comprising the fusion polypeptide of claim 101 and a pharmaceutically acceptable carrier.
- 103. (Previously presented) A dimer comprising two of the fusion polypeptides of claim 101.
- 104. (Previously presented) An expression vector comprising the nucleic acid molecule of claim 92.
- 105. (Previously presented) A host-vector system for the production of a fusion polypeptide comprising the expression vector of claim 105, in a suitable host cell.
- 106. (Previously presented) The host-vector system of claim 105, wherein the host cell is a bacterial cell, yeast cell, insect cell, or mammalian cell.
- 107. (Previously presented) The host-vector system of claim 106, wherein the host cell is selected from the group consisting of *E. coli* and CHO.
- 108. (Previously presented) A method of producing a fusion polypeptide, comprising growing cells of the host-vector system of claim 105, under conditions permitting production of the fusion polypeptide and recovering the fusion polypeptide so produced.
- 109. (Previously presented) A dimeric vascular endothelial growth factor (VEGF) antagonist, comprising two fusion polypeptides, each fusion polypeptide comprising:
- (a) a VEGF receptor component consisting essentially of an immunoglobulin-like
 (Ig) domain 2 of a first VEGF receptor and Ig domain 3 of a second VEGF receptor; and
 (b) a multimerizing component.
- 110. (Previously presented) The dimeric antagonist of claim 109, wherein the first VEGF receptor component is Flt1.
- 111. (Previously presented) The dimeric antagonist of claim 109, wherein the second VEGF receptor component is Flk1 or Flt4.
- 112. (Previously presented) The dimeric antagonist of claim 109, which is modified by acetylation or pegylation.
- 113. (Previously presented) A pharmaceutical composition, comprising the fusion polypeptide of claim 109 and a pharmaceutically acceptable carrier.
- 114. (Previously presented) A method of inhibiting vascular endothelial growth factor (VEGF) activity in a mammal, comprising administering the pharmaceutical composition of claim 113.

USSN10/009,852 Restriction Requirement dated 12 Aug 2004 Response dated 27 August 2004

- 115. (Previously presented) The method of claim 114, wherein the mammal is a human.
- 116. (Previously presented) A method of inhibiting tumor growth in a mammal, comprising administering the pharmaceutical composition of claim 113.
- 117. (Previously presented) A fusion polypeptide, comprising:
- (a) a VEGF receptor component consisting essentially of an immunoglobulin-like(lg) domain 2 of a first VEGF receptor and lg domain 3 of a second VEGF receptor; and(b) a multimerizing component.
- 118. (Previously presented) The fusion polypeptide of claim 117, wherein the first VEGF receptor component is Flt1.
- 119. (Previously presented) The fusion polypeptide of claim 117, wherein the second VEGF receptor component is Flk1 or Flt4.
- 120. (Previously presented) The fusion polypeptide of claim 117, wherein the multimerizing component comprises an immunoglobulin domain.
- 121. (currently amended) The fusion polypeptide of claim 120, wherein the immunoglobulin domain is selected from the group consisting of the Fc domain of IgG, and the light chain of IgG.
- 122. (Previously presented) The fusion polypeptide of claim 117, comprising the amino acid sequence of SEQ ID NO:12 or 16.
- 123. (Previously presented) A method of producing a fusion polypeptide which specifically binds a target protein, comprising the steps of:
- (a) identifying Ig domains of a first receptor protein which first receptor protein binds the target protein;
- (b) identifying Ig domains of a second receptor protein which second receptor protein binds the target protein;
- (c) producing a fusion protein of an lg domain of the first receptor protein and an lg domain of the second receptor protein;
 - (d) determining if the produced fusion protein binds the target protein; and
- (e) repeating (a)-(d) to obtain the fusion protein that specifically bind the target protein.
- 124. (Previously presented) The method of claim 123, wherein the first receptor protein is chosen from Flt1.
- 125. (Previously presented) The method of claim 123, wherein the second receptor protein is chosen from Flk1 and Flt4.
- 126. (Previously presented) The method of claim 123, wherein the fusion protein is produced by expression of operatively positioned nucleotide sequences encoding the Ig domain of the first and second receptor proteins.

- 127. (Previously presented) The method of claim 123, wherein the fusion protein further comprises an immunoglobulin domain.
- 128. (currently amended) The method of claim 127, wherein the immunoglobulin domain is chosen from the Fc domain of IgG, they and the heavy chain of IgG, and the light chain of IgG.
- 129. (Previously presented) The fusion protein produced by the method of claim 123.
- 130. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically acceptable amount of the fusion protein of claim 129.
- 131. (Previously presented) A method of treatment comprising administering to a patient a therapeutically effective amount of the composition of claim 130.